# PATENT SPECIFICATION

NO DRAWINGS

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**Int. Cl.:**—C 07 d 27/80

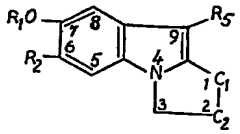
COMPLETE SPECIFICATION

## Pyrrolo[1,2-a]-Indoles

We, AMERICAN CYANAMID COMPANY, a corporation organised under the laws of the State of Maine, United States of America, of Berdan Avenue, Township of Wayne, New Jersey, United States of America, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it it to be performed, to be particularly described in and by the following statement:—

This invention relates to substituted pyrrolo[1,2-a] - indole compounds and to a process for the preparation thereof.

The present invention provides 6,7 - disubstituted and 7 - monosubstituted pyrrolo [1,2-a]indoles of the formula



... IA

wherein $R_5$ is a hydrogen atom or the group CHO and $C_1$ is $>CH_2$ or $>C=O$, and $C_2$ is $>CH_2$, $>CH$-carbalkoxy, $>CH$-carboxamido, or $>CH—C\equiv N$ and wherein $R_1$ is hydrogen, lower alkanoyl of 1 to 6 carbon atoms, lower alkyl of 1 to 6 carbon atoms or mononuclear aralkyl and $R_2$ is alkyl or hydrogen.

Also in accordance with this invention there is provided a process for preparing the compounds of formula IA, characterised by

(1) cyclising a 1-(β-substituted ethyl) indole - 2 - carboxylic acid or an ester, amide or nitrile derivative having the group $R_1O$ in the 5-position and the atom or group $R_2$ in the 6-position of the indole nucleus, in which the β-substituent is a carboxyl, a carboxylic acid ester or amide or a nitrile group, and wherein the 1 - (β-substituted ethyl) indole - 2 - carboxylic acid ester (or amide or nitrile derivative) may be prepared *in situ* by condensation of a 1-unsubstituted indole - 2 - carboxylic acid ester (or amide or nitrile derivative) and acrylonitrile or an acrylic acid ester or amide,

and, if desired, doing one or more of the following:

(2) when the product of step (1) is the β-keto ester heating with acid to decarbalkoxylate and form the corresponding 1-ketopyrrolo [1,2-a] indole

(3) treating the product of step (2) with hydrazine in the presence of a base to give the 2,3 - dihydro - 1H - pyrrolo [1,2-a] indole

(4) formylating the product of either step (2) or (3) to give the corresponding 9-formyl derivative.

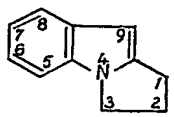
The cyclisation in step (1) can be effected by means of heating with a lower alkanoic acid anhydride and the starting material is a 1 - (β - carboxyethyl) indole - 2-carboxylic acid and the final product is the corresponding 1 - keto - pyrrolo [1,2-a] indole.

[*Price 4s. 6d.*]

Also, the cyclisation in step (1) can be effected by means of a basic condensation catalyst and the starting material is a 1 - (β - substituted ethyl) - indole - 2 - carboxylic acid ester (or amide or nitrile derivative) in which the β-substituent is a carboxylic acid ester, or amide or a nitrile group.

It is particularly preferred that when the 1 - (β - substituted ethyl) indole - 2 - carboxylic acid amide is used, the nitrogen atom of the amide group is a tertiary nitrogen.

The numbering system for the ring positions of the compounds of this invention can be indicated as follows:




The substituted pyrrolo[1,2-a] indoles of this invention are useful antimicrobial agents and are active *in vitro* against a variety of microorganisms including gram-positive and gram-negative bacteria and fungi. Typical compounds of the invention inhibit growth *in vitro* of such organisms as *Mycobacterium smegmatis* ATCC 607, *Staphylococcus aureus* ATCC 6548P, *Streptococcus faecalis* ATCC 8043, *Bacillus subtilis* ATCC 6633, *Proteus vulgaris* ATCC 9484, *Fusarium episphaeria* F-105, *Hormodendrum cladosporoides* Z-516, *Trichophyton mentagrophytes* E-11, *Microsporum gypseum* E-28, *Memnoniella echinata* Z-583, and *Chaetomium globosum* H-71.

The novel substituted pyrrolo[1,2-a]indoles of this invention are also useful as intermediates for the preparation of the antibiotic compounds which are described and claimed in our Patent Specification No. 1,010,771.

The pyrrolo [1,2-a]indole system is obtained by condensation of a 1-unsubstituted-2 - carbalkoxyindole (I) with an α,β-unsaturated carbonyl or nitrile derivative, such as an alkyl acrylate, acrylonitrile, or acrylamide in the presence of a basic catalyst, such as various metal alkoxides, metal hydroxides, and quaternary ammonium hydroxides, are representative bases, we prefer, however, trimethylbenzyl ammonium hydroxide or potassium t-butoxide. When this condensation is carried out in the presence of water the product is usually the 1 - (β - substituted ethyl) - 2 - carbalkoxyindole (II). This derivative can then undergo a Dieckman cyclization (base - catalysis) to give the pyrrolo [1,2-a]indole system (III). When the addition reaction is carried out in a non-aqueous solvent, such as benzene, the pyrroloindole β-keto ester, nitrile or amide is usually obtained directly in one operation. The β-keto ester, on heating with acid, preferably 95% acetic acid, will undergo decarbalkoxylation to a 1-ketopyrrolo [1,2-a] indole (IV). An alternate procedure to the pyrrolo[1,2-a]indole system involves treatment of a 2-carboxy - 1 - (β - carboxyethyl)indole (IIa) with hot acetic anhydride in the presence of potassium cyanide followed by treatment with dilute base, e.g. 5% ethanolic potassium hydroxide solution. This procedure affords a 1 - ketopyrrolo[1,2-a]indole (IV) directly.

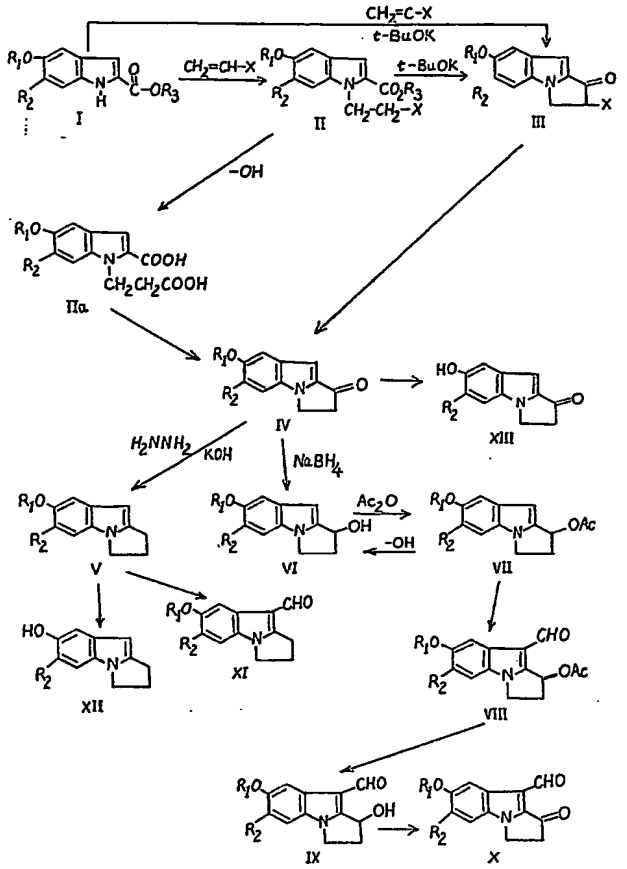
The 1-keto function may be reduced to a methylene group by the Wolf-Kishner procedure (IV→V) and to an alcohol by treatment with a metal hydride such as sodium borohydride (e.g. IV→VI). Acylation of the resulting 1 - hydroxypyrroloindole affords the corresponding ester (VI→VII) which may be hydrolized to reform the free alcohol (VII→VI, VIII→IX). The 1 -hydroxy group may also be oxidized to a keto function (IX→X). A useful reagent for this purpose is a solution of chromic oxide in pyridine.

Pyrroloindoles with a formyl group at the 9-position can be prepared via electrophilic substitution, i.e. formylation, of a 9-unsubstituted - pyrrolo [1,2-a] - indole (V→XI, VII→VIII). The preferred procedure for formylation involves treatment of the pyrroloindole with phosphorus oxychloride and dimethylformamide or N - methylformanilide. The resulting 9-formyl derivative may undergo further transformations.

1 - Keto - 9 - formyl derivatives (X) may be prepared by preferential oxidation with chromic oxide in pyridine of the 1 - hydroxy group in 1 - hydroxy - 9 - formyl derivatives (IX).

Using the appropriately 5- and 6-unsubstituted indole 2 - carbalkoxy derivative affords the corresponding 6- and 7-substituted pyrroloindole. The 7-hydroxy derivatives are obtained by hydrogenolysis of the 7 - benzyloxy group or by treatment of a 7-methoxy derivative with aluminium chloride in a refluxing inert solvent such as xylene, (V→XII, IV→XIII).

The following series of equations illustrates the above-discussed transformations. In the formulae, $R_1$ represents alkyl and aralkyl, $R_2$ represents hydrogen, alkyl, $R_3$ represents alkyl and $R_4$ represents alkyl.




This invention is further illustrated in conjunction with the following specific Examples. These Examples describe the preparation of the following compounds:

Example

1(a): Dimethyl - 4 - nitroanisole

1(b): 5 - Methoxy - 4 - methyl - 2 - nitrophenylpyruvic acid

1(c): 5 - Methoxy - 4 - methyl - 2 - nitrophenylpyruvic acid

1(d): 5 - Methoxy - 6 - methyl - 2 - indolecarboxylic acid

1(e): Methyl 5 - methoxy - 6 - methyl - 2 - indole carboxylate

1(f): Methyl 1 - ($\beta$ - cyanoethyl) - 5 - methoxy - 6 - methyl - 2 - indolecarboxylate

1(g): 2,3 - Dihydro - 7 - methoxy - 6 - methyl - 1 - oxo - 1H - pyrrolo[1,2-a] indole - 2 - carbonitrile

2: 2,3 - Dihydro - 7 - methoxy - 6 - methyl - 1 - oxo - 1H - pyrrolo[1,2-a] indole - 2 - carbonitrile

3: Methyl 2,3 - dihydro - 7 - methoxy - 6 - methyl - 1 - oxo - 1H - pyrrolo [1,2-a]indole - 2 - carboxylate

4: Condensation of Ethyl 5 - benzyloxy - 2 - indole - carboxylate with ethyl acrylate

5(a): 4 - Benzyloxy - 2,5 - dimethylnitrobenzene

5(b): Ethyl 5 - benzyloxy - 4 - methyl - 2 - nitrophenyl pyruvate

5(c): Ethyl 5 - benzyloxy - 6 - methyl - 2 - indole carboxylate

5(d): Methyl and ethyl ester of 7 - benzyloxy - 2,3 - dihydro - 6 - methyl - 1-oxo - 1H - pyrrolo[1,2-a]indole - 2 - carboxylic acid
6: 2,3 - Dihydro - 7 - methoxy - 6 - methyl - 1 - oxo - 1H - pyrrolo[1,2-a] indole
7: 2,3 - Dihydro - 7 - methoxy - 6 - methyl - 1 - oxo - 1H - pyrrolo[1,2-a] indole
8: 7 - Benzyloxy - 2,3 - dihydro - 1 - oxo - 1H - pyrrolo[1,2-a]indole
9: 7 - Benzyloxy - 2,3 - dihydro - 1 - oxo - 1H - pyrrolo[1,2-a]indole
10: 7 - Benzyloxy - 6 - methyl - 1 - oxo - 1H - pyrrolo - [1,2-a]indole
11: 2,3 - Dihydro - 7 - methoxy - 6 - methyl - 1H - pyrrolo[1,2-a]indole
12: 7 - Benzyloxy - 2,3 - dihydro - 1H - pyrrolo[1,2-a]indole
13(a): 7 - Benzyloxy - 2,3 - dihydro - 1 - hydroxy - 1H - pyrrolo[1,2-a]indole
13(b): 1 - Acetoxy - 7 - benzyloxy - 2,3 - dihydro - 1H - pyrrolo[1,2-a]indole
13(c): 1 - Acetoxy - 7 - benzyloxy - 9 - formyl - 2,3 dihydro - 1H - pyrrolo [1,2-a]indole
13(d): 7 - Benzyloxy - 9 - formyl - 2,3 - dihydro - 1 - hydroxy - 1H - pyrrolo [1,2-a]indole
13(e): 7 - Benzyloxy - 9 - formyl - 2,3 - dihydro - 1 - oxo - 1H - pyrrolo[1,2-a] indole
14: 2,3 - Dihydro - 9 - formyl - 7 - methoxy - 6 - methyl - 1H - pyrrolo[1,2-a] indole
15: 7 - Benzyloxy - 9 - formyl - 2,3 - dihydro - 1H - pyrrolo[1,2-a]indole
16: 2,3 - Dihydro - 9 - formyl - 7 - hydroxy - 6 - methyl - 1H - pyrrolo[1,2-a] indole
17: 2,3 - Dihydro - 7 - hydroxy - 6 - methyl - 1 - oxo - 1H - pyrrolo[1,2-a] indole
18: 7 - Benzyloxy - 2,3 - dihydro - 1 - oxo - 1H - pyrrolo[1,2-a]indole - 2 - carboxamide
19: 7 - Benzyloxy - 2 - cyano - 2,3 - dihydro - 1 - oxo - 1H - pyrrolo[1,2-a]indole
20(a): 2 - Carboxy - 1 - (β - carboxyethyl) - 5 - methoxy - 6 - methylindole
20(b): Methyl 2 - carbomethoxy - 5 - methoxy - 6 - methyl - 1 - indolepropionate
20(c): 2 - Carboxy - 1 - (β - carboxyethyl) - 5 - methoxy - 6 - methylindole
20(d): 2,3 - Dihydro - 7 - methoxy - 6 - methyl - 1 - oxo - 1H - pyrrolo[1,2-a] indole
21(a): Ethyl 5 - benzyloxy - 1 - (β - carbethoxyethyl) - 6 - methyl - 2 - indole-carboxylate
21(b): Ethyl 7 - benzyloxy - 2,3 - dihydro - 6 - methyl - 1 - oxo - 1H - pyrrolo [1,2-a]indole - 2 - carboxylate

EXAMPLE 1

(a) A well stirred suspension of 16.7 g (0.1 mole) of 2,5 - dimethyl - 4 - nitrophenol (R. L. Datta and P. S. Varma, J. Am. Chem. Soc., *41*, 2042 (1919)) in 50 ml of water at 40—45° is treated alternately and in portions with a solution of 7.0 g of sodium hydroxide in 18 ml of water and 12 ml of methyl sulphate. After 2 hours the mixture is filtered, and the solid is recrystallised from dilute methanol to give 14.5 g (80%) of needles, m.p. 90—92°C.

(b) Potassium *t*-butoxide is prepared by allowing 9.80 g (0.25 g atom) of potassium to react with 200 ml of *t*-butyl alcohol. The excess alcohol is removed by distillation. Benzene (100 ml) is added and removed in the same manner twice. The base is slurried in 200 ml benzene and 42.80 g of ethyl oxalate is added with mechanical stirring. A solution of 45.25 g (0.25 mol) of 2,5 - dimethyl - 4 - nitroanisole (a) in 600 ml of benzene is distilled until the boiling point is 80°C; the residual solution is cooled to room temperature and added to the stirred reaction solution. Within minutes a deep red solid separates; the mixture is mechanically stirred at reflux temperature for 24 hours and then at room temperature for 63 hours. The mixture is filtered and the residue is washed with ether and air-dried. The powder is dissolved in about 1 litre of water, treated with about 40 g of sodium bicarbonate and heated on the steam bath for 30 min. Acidification of the solution with hydrochloric acid gives 45.6 g (72%) of crystals, m.p. 106—108°C.

(c) Ethanol (6.25 ml) is added to a mechanically stirred slurry of 2.15 g (0.055 g atoms) of potassium in benzene. After all of the potassium reacts, the solvents are removed by distillation, benzene (50 ml) is added and removed in the same manner. The cooled residue is slurried in 100 ml of ether and treated with 7.3 g (0.05 mol, 6.75 ml) of ethyl oxalate. To the resulting solution is added a solution of 9.05 g (0.05

mol) of 2,5 - dimethyl 4 - nitroanisole (a) in 150 ml of ether. A red solid separates immediately and the mixture is mechanically stirred at room temperature for 18 hours, and then at reflux temperature for 4 hours. The mixture is filtered, and the solid is washed with ether. The residue is dissolved in water and the solution is heated on the steam bath for 30 minutes. The solution is cooled and extracted with ether. The aqueous solution is acidified with hydrochloric acid and filtered to give 6.123 g (49%) of crystals, m.p. 167—170°C.

From the ether extracts there is recovered 3.11 g (34%) of starting material.

(d) A solution of 42.0 g (0.166 mol) of 5 - methoxy - 4 - methyl - 2 - nitrophenylpyruvic acid (b) in 230 ml of 17% ammonium hydroxide and 115 ml of water is treated with a hot solution containing 300 g of ferrous sulphate heptahydrate in 340 ml of water. The mixture is mechanically stirred at steam-bath temperature for 1 hour and then allowed to cool to room temperature and filtered.

The residue is washed with dilute ammonium hydroxide until a test portion becomes only milky on acidification. The combined filtrate and washings are acidified with hydrochloric acid and the solid which separates is collected by filtration. The moist solid is recrystallised from dilute acetic acid to give 19.0 g (56% yield) of light brown solid, m.p. 240—242° (gas evolution).

(e) A solution of 38.7 g (0.188 mol) of 5 - methoxy - 6 - methyl - 2 - indolecarboxylic acid (d) and 1000 ml of methanolic hydrogen chloride is heated at reflux temperature for 3 hours. The solvent is removed under reduced pressure, and the residue is dissolved in about 1 litre of ether. This solution is treated with activated carbon, the mixture is filtered and the filtrate is taken to dryness. Recrystallisation of the residue from dilute methanol gives in two crops 38.6 g of white needles, m.p. 149—150°.

(f) A solution of 0.860 g ((3.92 mmols) of methyl 5 - methoxy-6 - methyl - 2 - indolecarboxylate (e) and 0.212 g (4.0 mmols) of acrylonitrile in 15 ml of dioxane containing 0.5 ml of 35% aqueous benzyl trimethyl solution is then allowed to stand at room temperature for 16 hours, diluted with water containing acetic acid and extracted with chloroform. The extract is dried over magnesium sulphate and taken to dryness. Crystallisation of the residual gum from methanol ammonium hydroxide is heated at 50°C with magnetic stirring for 30 minutes. The gives 0.500 g (48%) of white crystals, m.p. 99—101°C. Two recrystallisations from dilute methanol furnishes white rods, m.p. 119—121° C; $\lambda_{max}^{CH_3OH}$ 301 mμ (ε = 22,100); $\lambda_{max}^{KBr}$ 4.45, 5.86, 6.57, 7.95, 8.20, 8.30 μ.

(g) Potassium *t*-butoxide is prepared in the usual manner from 0.223 g (5.7 mg atoms) of potassium and 25 ml of *t*-butyl alcohol. A mechanically-stirred suspension of the base in 25 ml of benzene is treated with a solution of 1.550 g (5.7 mmols) of methyl 1 - (β - cyanoethyl) - 5 - methoxy - 6 - methyl - 2 - indole carboxylate (f) in 50 ml of benzene. The resulting mixture is stirred at reflux temperature for 24 hours and then at room temperature for 16 hours. The mixture is treated with cracked ice and acidified with dilute hydrochloric acid solution. After distribution of the reaction mixture between methylene chloride and additional water, the organic layer is dried over magnesium sulfate and taken to dryness. The residue is recrystallized from methanol to give 0.917 g. (67%) of crystals, m.p. 215—219°C. Several recrystallizations from methanol gives needles, m.p. 219—221°C; $\lambda_{max}^{CH_3OH}$ 336 mμ (ε = 21,800); $\lambda_{max}^{KBr}$ 4.44, 5.75, 6.50, 8.26 μ.

## Example 2

To a suspension of potassium t-butoxide, prepared from 0.880 g. (22.5 mg. atoms) of potassium and 50 ml. of *t*-butyl alcohol, in 50 ml. of benzene is added, with mechanical stirring, a solution of 4.923 g. (225 mmoles) of methyl 5 - methoxy - 6 - methyl - 2-indole - carboxylate (Example 1(e)) in 150 ml. of benzene and then 1.190 g. (22.5 mmoles, 1.47 ml.) of acrylonitrile. The resulting mixture is heated at reflux temperature for 6 hrs., acidified with 5% hydrochloric acid solution and extracted with methylene chloride. The combined organic extracts are dried over magnesium sulfate and taken to dryness. The residue is recrystallized twice from methanol to give 1.35 g. (25%) of crystals, m.p. 215—218°C.

## Example 3

A mechanically stirred suspension of potassium *t* - butoxide (prepared from 0.391 g., 10 mg.-atoms of potassium and 25 ml. of *t*-butyl alcohol) in 25 ml. of benzene is treated with a solution of 2.190 g. (10 mmoles) of methyl 5 - methoxy - 6-methyl - 2 - indole - carboxylate (Example 1(e)) in 50 ml. of benzene followed by 0.860

g (10 mmoles, 0.89 ml.) of methylacrylate. The mixture is heated at reflux temperature for 2 hrs. and then stirred at room temperature for 63 hrs. The reaction is diluted with water, acidified with hydrochloric acid solution and extracted with methylene chloride. The organic solution is dried over magnesium sulfate and taken to dryness. The residue is triturated with methanol and filtered to give 1.725 g. (63%) of near white crystals, m.p. 175—179°. Two recrystallizations from acetone - petroleum ether (b.p. 60—70°) give needles, m.p. 180—182°S; $\lambda_{max}^{CH_3OH}$ 336 mμ (ε=21,800); $\lambda_{max}^{KBr}$ 5.78, 6.52, 8.04, 8.25, 8.56 μ.

EXAMPLE 4

A mechanically stirred mixture of 100 g. (0.342 mole) of ethyl - 5 - benzyloxy - 2-indolecarboxylate, 38.3 g. (0.342 mole) of potassium *t* - butoxide and 29.5 g. (0.342 mole, 30.6 ml.) of methyl acrylate in 2300 ml. of benzene is heated at reflux temperature for 4 days. The cooled mixture is acidified with dilute hydrochloric acid solution, whereupon all solid dissolved. The aqueous layer is extracted with methylene chloride, and the dried combined organic layers are concentrated. As a quantity of solid sufficient enough to cause bumping separates, it is removed by filtration and concentration of the filtrate is continued. In this manner the following six fractions are obtained: (a) 39.7 g. of *ethyl 7 - benzyloxy - 2,3 - dihydro - 1 - oxo - 1H - pyrrolo[1,2-a]indole - 2 - carboxylate,* m.p. 160—164°; (b) 15.4 g. of *methyl 7 - benzyloxy - 2,3 - dihydro - 1 - oxo-1H - pyrrolo[1,2-a]indole - 2 - carboxylate,* m.p. 142—145°C; (c) 2.0 g. of methyl ester, m.p. 142—145°; (d) 7.5 g. of starting indole ester, m.p. 160—162°C; (e) 3.4 g. of methyl ester, m.p. 142—145°C; and (f) 5.5 g. of starting indole ester. These amounts represent a 33% yield of ethyl ester, an 18% yield of methyl ester and a 13% recovery of starting indole ester.

The ethyl ester is recrystallized three times from ethanol to give white plates, m.p. 151—153°C; $\lambda_{max}^{CH_3OH}$ 325 mμ (ε=23,000); $\lambda_{max}^{HCl}$ 330 mμ (ε=24,100); $\lambda_{max}^{NaOH}$ 356 mμ (ε=26,500); $\lambda_{max}^{KBr}$ 5.71, 5.84, 6.15, 6.50, 8.35 μ.

A sample of methyl ester is recrystallized two times from methanol to give shining plates, m.p. 140—142°C; $\lambda_{max}^{CH_3OH}$ 325 mμ (ε=22,800); $\lambda_{max}^{NaOH}$ 356 mμ (ε=26,400); $\lambda_{max}^{KBr}$ 5.69, 5.84, 6.14, 6.48, 8.30—8.35 μ.

EXAMPLE 5

(a) 2,5 - dimethyl - 4 - nitrophenol (16.7 g, 0.1 mol) is added to a suspension of sodium methoxide (6.0 g) in anhydrous t-butanol (75 ml) with stirring. Benzyl chloride (12.7 g) is added to the mixture followed by t-butanol (50 ml). After 2 hours refluxing, the mixture contains orange solid and the pH is 9. An additional portion of benzyl chloride (12.7 g) is added and then methanol (90 ml) which dissolves much of the solid. After 4 more hours, of refluxing the pH is 6 and sodium methoxide (3.0 g) is added and the mixture is refluxed and stirred overnight. Then the pH is 4—6 and sodium methoxide (3.0 g) is again added. After 3 more hours of refluxing the mixture is cooled to give long yellow needles which are washed with 10% sodium hydroxide until the filtrate is clear. The alcohol filtrate is saved. An ether solution of the solid is washed with 10% sodium hydroxide (100 ml), dried, and evaporated *in vacuo,* with the bath temperature maintained at 30—40°C, to give 14.3 g of residual solid.

The alcohol filtrate (above) is concentrated *in vacuo* to a mixture of oil and solid which is dissolved in ether. The ether solution is extracted with 14 100 ml portions of 10% sodium hydroxide until the aqueous layer is colourless. The ether layer is dried and concentrated *in vacuo* to a dark brown oil containing a solid. After refrigeration the solid is filtered and washed with hexane to give 5.5 g of light orange solid. No additional solid is obtained by treating the filtrate with hexane. The solid recrystallises from boiling hexane (350 ml, charcoal) to give light yellow solid (18.3 g) (92.19%), m.p. 86—87°C.

(b) Freshly distilled ethyl oxolate (32.64 g, .223 mol) is slowly added to a fine suspension of freshly prepared potassium *t*-butoxide (25.26 g, 0.233 mol) in dry benzene (150 ml) to give a yellow solution which clears completely on warming. A benzene solution (150 ml) of 4 - benzyloxy - 2,5 - dimethyl - nitrobenzene (a) (28.71 g, .1116

mol) is rapidly added to the mixture and a deep red precipitate forms immediately. The mixture is stirred at reflux for 2½ hours and then it is cooled, filtered, and pressed dry. The benzene filtrate is reserved. The solid is washed several times with anhydrous ether, until the filtrate is colourless, to give a bright scarlet powder. The potassium salt is dissolved in glacial acetic acid (150 ml) and on cooling a pale yellow solid is obtained from the solution which is washed with water until the pH of the filtrate is 6—7. After drying *in vacuo* at 50—60°C for 1 hour, 0.89 g (75%) of the pale yellow ester, m.p. 88—90°C, is obtained. Recrystallisation from 40% benzene—60% hexane (charcoal) gives a nearly colourless solid, m.p. 90—92°C.

(c) Pale yellow ethyl 5 - benzyloxy - 4 - methyl - 2 - nitrophenylpyruvate (b) (5.0 g, .024 mols), m.p. 88—90°, is dissolved in boiling glacial acetic acid (60 ml) to give a light yellow-brown solution. Zinc dust (20 g) is added slowly over a 5 min. period and the mixture turns dark brown. After 5 minutes boiling the colour lightens to a red-brown colour and the mixture is boiled for an additional 10 minutes and then filtered while hot. A pale yellow-amber crystalline solid (1.98 g, 46%), m.p. 110—138°, is obtained by careful dilution of the filtrate with an equal volume of water. Additional product is obtained by further dilution of the mother liquor.

The crude solid is dissolved in anhydrous ether and separated from any insoluble material by filtration. The ether solution is chromatographed on Merck reagent grade alumina in a 30 mm column. The ether eluant is evaporated to give a yellow - white solid which on recrystallisation from acetone Skellysolve B gives pale needles, m.p. 143—144°C.

(d) A mixture of the methyl and ethyl ester is prepared by reacting freshly prepared potassium *t* - butoxide, ethyl 5 - benzyloxy - 6 - methyl - 2 - indolecarboxylate and methyl acrylate in dry benzene according to the procedure described in Example 3 for the analogous 7 - methoxy compound. The reaction mixture is refluxed for 3½—4 days and then it is acidified and extracted with methylene chloride. After drying, the organic layer is concentrated *in vacuo* to a solid which on trituration with methanol gives white needles, m.p. 149—153°C. (methanol), $\lambda_{max}^{CH_3OH}$ 335 mμ; $\lambda_{max}^{KBr}$ 5.72, 5.86, 8.35 μ; positive ferric chloride enol test.

EXAMPLE 6

A mixture of 3.00 g (11 mmoles) of methyl 2,3 - dihydro - 7 - methoxy - 6 - methyl - 1 - oxo - 1H - pyrrolo[1,2-a]indole - 2 - carboxylate (Example 3), 120 ml. of methanol and 30 ml. of 37% hydrochloric acid solution is heated at reflux temperature for 1 hr. The solid dissolves during this period, and the resulting green solution is poured into much water and extracted with methylene chloride. The extracts are washed with sodium bicarbonate solution, dried over magnesium sulfate and taken to dryness. The residue is slurried with 50 ml. of ether and filtered to give 1.462 g. of tan solid, m.p. 204—208°C. This material is recrystallized from acetone-petroleum ether (b.p. 60—70°) to give 1.000 g. (42%) of yellow crystals, m.p. 211—213°C. Two additional recrystallizations from acetone gives yellow crystals, m.p. 213—215°C; $\lambda_{max}^{CH_3OH}$ 331 mμ (ε = 21,200); $\lambda_{max}^{KBr}$ 5.82, 6.49, 8.21, 8.40 μ.

EXAMPLE 7

A solution of 37.7 g. (0.138 moles) of methyl 2,3 - dihydro - 7 - methoxy - 6-methyl - 1 - oxo - 1H - pyrrolo[1,2-a]indole - 2 - carboxylate (Example 3) in 800 ml. of 95% acetic acid is heated at reflux temperature for about 18 hours. The solution is cooled and filtered to give 23.2 g. of crystals, m.p. 216—218°. The filtrate is diluted with much water, and the precipitated solid is recrystallized from methylene chloride-petroleum ether (b.p. 30—60°C) to give 2.4 g (86% total yield) of crystals, m.p. 210—215°C.

EXAMPLE 8

A mixture of 0.500 g. (1.5 mmoles) of methyl 7 - benzyloxy - 2,3 - dihydro - 1-oxo - 1H - pyrrolo[1,2-a]indol - 2 - carboxylate (Example 4), 40 ml. of methanol and 10 ml. of 37% hydrochloric acid is heated at reflux for 1 hr. The product is isolated with methylene chloride and recrystallized from acetone - petroleum ether (b.p. 60—70°) to give 155 mg. (38%) of crystals, m.p. 181.0—183.5°C. Three recrystallizations from the same solvent pair gives yellow plates, m.p. 183—184°C; $\lambda_{max}^{CH_3OH}$ 320 mμ (ε = 20,500); $\lambda_{max}^{KBr}$ 5.84, 5.90 (split carbonyl), 6.15, 6.48 μ.

EXAMPLE 9

A solution of 45.2 g. (0.13 mole) of ethyl 7 - benzyloxy - 2,3 - dihydro - 1 - oxo-1H-pyrrolo[1,2-a]indole - 2 - carboxylate (Example 4) and 20.8 g. (0.062 mole) of methyl 7 - benzyloxy - 2,3 - dihydro - 1 - oxo - 1H - pyrrolo[1,2-a]indole - 2 - carboxylate in 1600 ml. of 95% acetic acid is heated at reflux temperature for 16 hrs.; isolation of the product as described for the methoxy methyl ketone (Example 7) gives 45.0 g. (85% yield) of shiny plates, m.p. 186—188°C.

EXAMPLE 10

The previously described mixture of ethyl and methyl carboxylates (Example 5(d)) is refluxed for 18 hrs. in 95% glacial acetic acid. A tan solid is collected from the dark brown solution on cooling and dilution with water in 70% yield, m.p. 197—199.5°C. (dec.); $\lambda_{max}^{CH_3OH}$ 331 mμ; $\lambda_{max}^{KBr}$ 5.87, 8.36μ.

EXAMPLE 11

A mixture of 2,3 - dihydro - 7 - methoxy - 6 - methyl - 1 - oxo - 1H - pyrrolo [1,2-a]indole (Example 6, 7) (1.67 g.; 7.75 mmoles) and 99—100% hydrazine hydrate (0.8 ml.) in diethylene glycol (30 ml.) containing 85% potassium hydroxide (1.120 g.) is refluxed, with stirring, for 4 hrs. The reaction mixture is aged in the cold for 1 hr. and filtered to give 690 mg., of a grey solid, m.p. 115—124°. The filtrate is extracted with methylene chloride. The extract is dried over anhydrous sodium sulfate and taken to dryness. Crystallization of the residue from methanol gives 77 mg. of light yellow crystals, m.p. 116—121°C, to give a total yield of 767 mg. (49%). Recrystallization from petroleum ether (30—60°) furnishes light yellow crystals, m.p. 116—118°C; $\lambda_{max}^{CH_3OH}$ 279, 295 (sh), 308 (sh) mμ (ε = 7930, 6930, 4620); no carbonyl absorbtion in the infrared.

EXAMPLE 12

A mixture of 831 mg. (3.0 mmoles) of 7 - benzyloxy - 2,3 - dihydro - 1 - oxo - 1H - pyrrolo[1,2-a]indole (Examples 8, 9), 0.4 ml. of hydrazine hydrate, 560 mg. of potassium hydroxide and 10 ml. of diethylene glycol is heated at reflux temperature for 4 hrs. The cooled mixture is poured into water and extracted with methylene chloride. The dried extract is evaporated, and the residue is dissolved in benzene and passed through a "Florisil" (a synthetic magnesium silicate) column. The word "Florisil" is a registered Trade Mark. The solid in the first 50 ml. of benzene eluate is recrystallized from acetone - petroleum ether (b.p. 60—70°C) to give 0.207 g. (27%) of white crystals, m.p. 147—150°C. Three recrystallisations from methanol gives white crystals, m.p. 150—152°C; $\lambda_{max}^{CH_3OH}$ 278, 296(sh), 308(sh) mμ (ε = 8150; 6850; 3160); no carbonyl absorption in the infrared.

EXAMPLE 13

(a) A mixture of 2.77 g (10 mmols) of 7 - benzyloxy - 2,3 - dihydro - 1 - oxo - 1H-pyrrolo[1,2-a]indole (Examples 8, 9) and 250 ml of ethanol is heated to reflux temperature. The hot suspension is treated with 0.756 g (20 mmoles) of sodium borohydride; all solid immediately dissolves. The solution is heated at reflux temperature for 2 minutes and then left at room temperature for 1 hour. The solvent is removed, and the residue is distributed between 1% sodium hydroxide solution and methylene chloride. The organic layer is dried over magnesium sulphate and taken to dryness. The residue is recrystallised from acetone - petroleum ether (b.p. 60—70°C) with the aid of activated charcoal to give 1.84 g (66% yield) of crystals, m.p. 121—124°C. Several recrystallisations from ether - petroleum ether (b.p. 60—70°C) and then benzene - petroleum ether (b.p. 60—70°C) gives needles, m.p. 122.0—12.5°; $\lambda_{max}^{CH_3OH}$ 278, 298(sh), 310(sh) mμ (ε = 10.700; 6,150; 4,110); $\lambda_{max}^{KBr}$ 2.98; 6.13; 6.33, 6.43, 8.50 μ.

(b) A solution of 1.97 g (7.1 mmol) of 7 - benzyloxy - 2,3 - dihydro - 1 - hydroxy-1H - pyrrolo[1,2-a]indole (a) in 25 ml of acetic anhydride is treated with 1.15 g (14 mmol) of sodium acetate and the resulting mixture is heated on a steam bath for 1.5 hour. After this mixture is cooled and poured onto ice it is stirred until all of the acetic anhydride is hydrolysed and the crystalline acetate is present. This acetate is collected and washed well with water, dissolved in methylene chloride, washed two times with potassium bicarbonate solution, dried and concentrated as petroleum ether (60—70°) is added. Cooling affords 1 - acetoxy - 7 - benzyloxy - 2,3 - dihydro - 1H - pyrrolo

[1,2-a]indole, white plates, m.p. 104—106°C; $\lambda_{max}^{KBr}$ 5.75(s), 8.0(s) $\mu$; $\lambda_{max}^{CH_3OH}$ 220 ($\epsilon$=9,300), 302 ($\epsilon$=4,300), 315 ($\epsilon$=2,900) m$\mu$. Further recrystallising from acetone-petroleum ether (60—70°), gives material with m.p. 109°C.

(c) To 1.0 ml of chilled dimethylformamide is added 306 mg (2 mmol, 0.2 ml) of freshly distilled phosphorous oxychloride. The mixture is stirred and cooled for 15 min., then treated with a solution containing 642 mg (2 mmol) of 1 - acetoxy - 7 - benzyloxy-2,3 - dihydro - 1H - pyrrolo[1,2-a]indole (b) in 5 ml of dimethylformamide, added dropwise. After the resulting yellow solution is stirred at ice-bath temperature for 2 hours it is poured onto a mixture of ice and 8 ml of 1N sodium hydroxide solution. The precipitate that forms is collected, washed with 1% sodium hydroxide solution, dissolved in methylene chloride solution, washed with potassium bicarbonate solution, dried and concentrated. Crystallisation of the residue from methanol affords 602 mg (87%) of 1 - acetoxy - 7 - benzyloxy - 9 - formyl - 2,3 - dihydro - 1H - pyrrolo [1,2-a]indole, white plates, m.p. 163—164°C; $\lambda_{max}^{KBr}$ 3.5(w), 3.6(w), 5.70(s), 6.10(s), 8.25(s) $\mu$; $\lambda_{max}^{CH_3OH}$ 215 ($\epsilon$=32,000), 257 ($\epsilon$=21,000), 276 ($\epsilon$=4,800), 308 ($\epsilon$=11,000) m$\mu$.

(d) To a solution of 7.5 g of sodium hydroxide in 10 ml of water and 140 ml of methanol is added 1.31 g (3.75 mmol) of 1 - acetoxy - 7 - benzyloxy - 9 - formyl-2,3 - dihydro - 1H - pyrrolo[1,2-a]indole (c). The resulting mixture is heated on a steam-bath for 20 min, cooled and concentrated to 20 ml. The concentrate is treated with ether - methylene chloride (1:1) and water. The organic layer is washed with potassium bicarbonate solution, dried and concentrated. Crystallisation of the residue from methanol, with charcoal decolorisation, affords 719 mg (58%) of 7 - benzyloxy-9 - formyl - 2,3 - dihydro - 1 - hydroxy - 1H - pyrrolo[1,2-a]indole, m.p. 126—130° C; $\lambda_{max}^{KBr}$ 2.9(s), 3.6(w), 3.7(w), 6.15(s) $\mu$; $\lambda_{max}^{CH_3OH}$ 216 ($\epsilon$=33,000), 257 ($\epsilon$=27,000), 275 ($\epsilon$=14,000), 308 m$\mu$ ($\epsilon$=13,000).

(e) An ice-cooled solution of 102 mg (0.33 mmol) of 7 - benzyloxy - 9 - formyl-2,3 - dihydro - 1 - hydroxy - 1H - pyrrolo - [1,2-a]indole (d) in 1 ml of pyridine is treated with a slurry of 100 mg (1.0 mmol) of chromium trioxide in 5 ml of pyridine. The mixture is stirred at 5° for 54 hours, then treated with water and methylene chloride. The methylene chloride layer is filtered, washed with potassium bicarbonate solution, dried and concentrated. Crystallisation of the residue from ethanol with charcoal decolorisation affords 48 mg (47%) of 7 - benzyloxy - 9 - formyl - 2,3 - dihydro-1 - oxo - 1H - pyrrolo[1,2-a]indole, m.p. 194—197°C; $\lambda_{max}^{KBr}$ 3.6(w), 3.7(w), 5.8(s), 6.10(s) $\mu$; $\lambda_{max}^{CH_3OH}$ 208 ($\epsilon$=32,000), 245 ($\epsilon$=20,000), 253 ($\epsilon$=21,000), 262 ($\epsilon$=15,000 280 ($\epsilon$=7,300), 343 m$\mu$ ($\epsilon$=16,000).

## Example 14

A mixture of N - methylformanilide (1.54 g., 0.0114 moles) and freshly distilled phosphorous oxychloride (1.76 g., 0.0114 moles) is stirred at room temperature for 15 min. Ethylene dichloride (10 ml.) is added and the reaction mixture is cooled to 0°. To the reaction mixture is added 1 g. (4.96 mmoles) of 2,3 - dihydro - 7 - methoxy-6 - methyl - 1H - pyrrolo[1,2-a]indole (Example 11) and the solution is heated at reflux for 20 min. The solution is cooled and is poured, with vigorous stirring, into 50 ml. of cold water containing 6 g. of sodium acetate. The solvent is removed by steam distillation and after chilling the mixture is filtered to give 985 mg. of a reddish solid, m.p. 190—192°C.

The filtrate is extracted with methylene chloride. The extract is dried over anhydrous sodium sulfate and then taken to dryness. Crystallization of the residue from methylene chloride - petroleum ether (30—60°) furnished white crystals, m.p. 195—197°C; $\lambda_{max}^{CH_3OH}$ 256 m$\mu$ ($\epsilon$=18,200), 282 m$\mu$ ($\epsilon$=16,800), 309 m$\mu$ ($\epsilon$=13,500); $\lambda_{max}^{KBr}$ 3.56, 3.66, 6.06, 6.5, 7.95 $\mu$.

## Example 15

To 0.5 ml. of ice-cooled dimethylformamide is added 71 mg. (0.47 mmole) of freshly distilled phosphorous oxychloride. The mixture is stirred and cooled for 15 min., then treated with a suspension of 122 mg (0.47 mmole) of 7 - benzyloxy - 2,3 - dihydro-

1H-pyrrolo[1,2-a]indole (Example 12) in a 2-ml. of dimethylformamide. The yellow solution that forms is stirred at 35°C for 1 hr., then poured onto ice. A pink solid (starting material) that precipitates is collected on a filter. The filtrate is made alkaline with dilute sodium hydroxide solution and the pale yellow solid that forms is washed with water and dried. In this manner there is obtained 65 mg (48%) of 7 - benzyloxy-9 - formyl - 2,3 - dihydro - 1H - pyrrolo - [1,2-a]indole, m.p. 157°C, $\lambda_{max}^{KBr}$ 3.6(w), 3.8(w), 6.2(s) $\mu$; $\lambda_{max}^{CH_3OH}$ 215 ($\epsilon$ = 33,000), 257 ($\epsilon$ = 20,000), 276 ($\epsilon$ = 14,000), 308 m$\mu$ ($\epsilon$ = 12,000).

EXAMPLE 16

A mixture of 2,3 - dihydro - 9 - formyl - 7 - methoxy - 6 - methyl - 1H - pyrrolo[1,2-a] - indole (Example 14) (3 g., 0.0131 mols) and aluminium chloride (3.4 g, 0.0256 mols) in xylene (140 ml) is refluxed with vigorous stirring for 5 hours. After cooling, the reaction mixture is poured onto ice and digested. The resulting red solid is filtered to give 2.36 g (84%), m.p. >300°C. Recrystallisation from a large volume of acetone furnishes white crystals, m.p. >300°C; $\lambda_{max}^{CH_3OH}$ 256 ($\epsilon$ = 15,910), 283 ($\epsilon$ = 14,910), 311 m$\mu$ ($\epsilon$ = 13,000); $\lambda_{max}^{KBr}$ 3.08, 3.35, 3.53, 6.1, 6.5, 8.05$\mu$.

EXAMPLE 17

A mixture of 645 mg (3 mmols) of 2,3 - dihydro - 7 - methoxy - 6 - methyl - 1-oxo - 1H - pyrrolo[1,2-a]indole (Examples 6,7) 800 mg (6 mmol) of anhydrous aluminium chloride and 20 ml of xylene is stirred in a nitrogen atmosphere and heated at reflux temperature for 5 hours. It is then cooled and decomposed with ice and dilute hydrochloric acid and extracted into ethyl acetate. The ethyl acetate solution is washed with water, dried and concentrated. The glassy solid residue (536 mg) is dissolved in 75 ml of the lower and 25 ml of the upper phase of the system 70 heptane : 30 ethyl acetate : 15 methanol : 6 water and mixed with 150 g of diatomaceous earth. This pack is placed atop a column (7.2 cm.dia.) of 700 g. of diatomaceous earth admixed with 350 ml of the lower phase described above, and the upper phase is passed through the column. The hold-back volume is 1700 ml. The effluent is passed through a recording ultraviolet spectrophotometer set at 330 m$\mu$. The product is contained in hold - back volumes 3.5—5.0. Concentrations of this effluent affords 139 mg (23%) of 2,3-dihydro-7 - hydroxy - 6 - methyl - 1 - oxo - 1H - pyrrolo[1,2-a]indole, orange powder, m.p. 255°C (dec.); $\lambda_{max}^{KBr}$ 3.05(s), 5.95(s)$\mu$; $\lambda_{max}^{CH_3OH}$ 216 ($\epsilon$ = 31,000), 332m$\mu$ ($\epsilon$ = 20,000).

EXAMPLE 18

Freshly prepared potassium *t*-butoxide is suspended in freshly distilled tetrahydrofuran. On addition of a tetrahydrofuran solution of an equimolar quantity of ethyl 5-benzyloxy - 2 - indolecarboxylate the suspended solid dissolves. An equimolar quantity of acrylamide is added to the solution which is then heated at reflux for 3 days. Within 1 hour, white solid precipitates. The reaction mixture is cooled, acidified with hydrochloric acid and the solvent is removed *in vacuo*. The hard amber residue is pulverised and extracted with boiling methylene chloride three times to leave a cream - coloured solid residue (61%). The solid is recrystallised from acetonitrile to give white lustrous plates, m.p. 228—9°C, $\lambda_{max}^{CH_3OH}$ 318 m$\mu$; $\lambda_{max}^{KBr}$ 3.57, 5.81, 6.04, 6.21, 6.58, 8.18$\mu$.

EXAMPLE 19

To a solution of potassium *t*-butoxide, prepared by dissolving 0.624 g (16 g at.) of potassium in 30 ml of *t*-butyl alcohol, is added a solution of 4.53 g (15.5 mmole) of ethyl 7 - benzyloxy - 2 - indolecarboxylate in 20 ml of *t* - butyl alcohol. The mixture is stirred for 15 minutes, treated with 0.85 g (16 mmol) of acrylonitrile, and heated at reflux temperature for 2 days. It is poured into water, acidified with dilute hydrochloric acid and the precipitate that results is washed with water and dried. Crystallisation of this precipitate from acetone - petroleum ether (60—70°) affords 2.35 g (53%) of 7 - benzyloxy - 2 - cyano - 2,3 - dihydro - 1 - oxo - 1H - pyrrolo[1,2-a]indole, pale yellow plates, m.p. 225—230°C; $\lambda_{max}$ 4.4 (C=N), 5.85 (C=O, s.) $\mu$; 328 ($\epsilon$ 21,000) m$\mu$.

EXAMPLE 20

(a) A suspension of 4.8 g (0.0176 mols) of methyl 1 - (β - cyanoethyl) - 5 - methoxy - 6 - methyl - 2-indolecarboxylate (Example 1(f)) in 100 ml. of 10% potassium hydroxide is refluxed, with stirring for 3 hours, during which time solution occurs. The reaction mixture is cooled, acidified with concentrated hydrochloric acid, and the precipitate is filtered to give 4.7 g of white solid, m.p. 230—231°C.

(b) A solution of 0.860 g (3.92 mmols) of methyl 5 - methoxy - 6 - methyl - 2-indolecarboxylate (Example 1(e)) and 0.344 g (4.00 mmols, 0.35 ml) of methyl acrylate in 15 ml of dioxane containing 0.5 ml of 35% aqueous benzyl trimethyl ammonium hydroxide is heated at 50°C for 30 minutes and then magnetically stirred at room temperature for 63 hours. The solution is diluted with water containing acetic acid and extracted with methylene chloride. The extract is dried and evaporated to give a residue which is crystallised from dilute methanol to give 0.311 g of methyl 5 - methoxy - 6-methyl - 2 - indolecarboxylate. Concentration of the mother liquor gives a solid with $\lambda_{max}^{KBr}$ 5.91, 6.60, 8.05, 8.25μ.

(c) By the procedure of Example 20(a), methyl-2-carbomethoxy - 5 - methoxy - 6-methyl - 1 - indolepropionate (Example 20(b)) is treated with a 10% potassium hydroxide solution to give the product as a white solid, m.p. 228—231°C.

(d) A solution of 900 mg. (3.14 mmoles) of 2 - carboxy - 1 - (β - carboxyethyl)-5 - methoxy - 6 - methyl indole (Example 20(a)) 60 mg. of potassium cyanide and 35 ml. of acetic anhydride is refluxed for 20 hours. The acetic anhydride is removed *in vacuo* and the residue is dissolved in a mixture of 25 ml. 10% potassium hydroxide and 25 ml. of ethanol. The solution is refluxed for one hour. The alcohol is removed *in vacuo* and the aqueous phase is extracted with methylene chloride. The organic phase is treated with decolorizing charcoal, dried over magnesium sulfate and is taken to dryness *in vacuo*. The residue is recrystallized from methylene chloride - petroleum ether (30—60°) to give white crystals, m.p. 210—215°C.

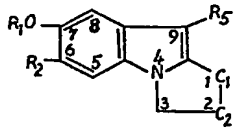
EXAMPLE 21

(a) A warm solution of ethyl 5 - benzyloxy - 6 - methyl - 2 - indolecarboxylate (Example 5(c)) in dry xylene is added to a well-stirred suspension of freshly prepared potassium tertiary - butoxide in dry xylene. Ethyl acrylate is added to the mixture which is refluxed for 40 hours. The mixture contains a solid which dissolves on acidification with 3 N hydrochloric acid. The mixture is extracted with methylene chloride and the organic layer is separated, dried, and concentrated to an oil that solidifies on treatment with methanol. The brown - yellow solid, m.p. 133—138°C (ethanol), is dissolved in ethanol (charcoal) and ether is added. The solvent is slowly evaporated to dryness and white silky needles, m.p. 87—88°, are separated from a hard yellow - brown solid.

(b) Ethyl 5 - benzyloxy - 1 - (β - carbethoxyethyl) - 6 - methyl - 2 - indolecarboxylate (a) is added to a stirred freshly-prepared suspension of potassium tertiary-butoxide in anhydrous benzene. The mixture is refluxed for four days. The reaction mixture is cooled, acidified with dilute hydrochloric acid, and then extracted with methylene chloride. The combined extracts are dried and then evaporated to dryness. The residual material is recrystallised twice from ethanol to give a white solid melting at 139—141°C.

WHAT WE CLAIM IS:—

1. A process for preparing 6,7 - disubstituted and 7 - monosubstituted pyrrolo [1,2-a]indoles of the formula



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wherein $R_5$ is a hydrogen atom or the group CHO and $C_1$ is $>C<_{H}$ or $>C=O$, and $C_2$ is $>CH_2$, $>CH$ - carbalkoxy, $>CH$ - carboxamido, or $>CH—C\equiv N$ and wherein $R_1$ is hydrogen, lower alkanoyl of 1 to 6 carbon atoms, lower alkyl of 1 to 6 carbon atoms or mononuclear aralkyl and $R_2$ is alkyl or hydrogen characterized by

(1) cyclizing a 1 - (β - substituted ethyl) indole - 2 - carboxylic acid or an ester,

amide or nitrile derivative having the group $R_1O$ in the 5-position and the group $R_2$ in the 6-position of the indole nucleus, in which the β-substituent is a carboxyl, a carboxylic acid ester or amide or a nitrile group, and wherein the 1 - (β - substituted ethyl) indole - 2 - carboxylic acid ester (or amide or nitrile derivative) may be prepared *in situ* by condensation of a 1 - unsubstituted indole - 2 - carboxylic acid ester (or amide or nitrile derivative) and acrylonitrile or an acrylic ester or amide, and if desired, doing one or more of the following:

(2) when the product of step (1) is the β-keto ester heating with acid to decarbalkoxylate and form the corresponding 1-ketopyrrolo[1,2-a] indole

(3) treating the product of step (2) with hydrazine in the presence of a base to give the 2,3 - dihydro - 1H - pyrrolo [1,2-a] indole

(4) formylating the product of either step (2) or (3) to give the corresponding 9-formyl derivative.

2. A process according to claim 1, wherein the cyclization is effected by means of heating with a lower alkanoic acid anhydride and the starting material is a 1 - (β-carboxyethyl) indole - 2 - carboxylic acid and the final product is the corresponding 1 - keto - pyrrolo [1,2-a] indole.

3. A process according to claim 1, wherein the cyclization is effected by means of a basic condensation catalyst and the starting material is a 1 - (β - substituted ethyl) - indole - 2 - carboxylic acid ester (or amide or nitrile derivative) in which the β-substituent is a carboxylic acid ester, or amide or a nitrile group.

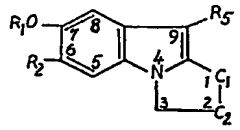
4. A process according to claim 1 or 3, wherein when the 1 - (β - substituted ethyl) indole - 2 - carboxylic acid amide is used, the nitrogen atom of the amide group is a tertiary nitrogen.

5. A process according to any one of claims 1, 3 or 4, wherein the basic condensation catalyst is a metal hydroxide, a metal alkoxide or a quaternary ammonium hydroxide.

6. A process for producing 6,7 - disubstituted and 7 - monosubstituted pyrrolo [1,2-a] indoles of formula IA substantially as described.

7. 6,7 - Disubstituted and 7 - monosubstituted pyrrolo [1,2-a]indoles of formula IA whenever prepared by the process substantially as described.

8. 6,7 - Disubstituted and 7 - monosubstituted pyrrolo [1,2-a] indoles of the formula:



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wherein $R_5$ is a hydrogen atom or the group CHO and $C_1$ is $>C<_{H}$ or $>C=O$, and $C_2$ is $>CH_2$, $>CH$ - carbalkoxy, $>CH$ - carboxamido, or $>CH—C\equiv N$ and wherein $R_1$ is hydrogen, lower alkanoyl of 1 to 6 carbon atoms, lower alkyl of 1 to 6 carbon atoms or mononuclear aralkyl and $R_2$ is alkyl or hydrogen.

9. 2,3-Dihydro-7-methoxy-6-methyl-1-oxo-1H-pyrrolo-[1,2-a]indole.

10. 7 - Benzyloxy - 2,3 - dihydro - 6 - methyl - 1 - oxo - 1H - pyrrolo - [1,2-a] indole.

11. 7 - Benzyloxy - 2,3 - dihydro - 1 - oxo - 1H - pyrrolo[1,2-a]-indole.

12. 7 - Benzyloxy - 2,3 - dihydro - 1 - oxo - 1H - pyrrolo[1,2-a]-indole - 2-carboxamide.

13. 2,3 - Dihydro - 7 - methoxy - 6 - methyl - 1H - pyrrolo[1,2-a] - indole.

14. 7 - Benzyloxy - 2,3 - dihydro - 9 - formyl - 1 - hydroxy - 1H - pyrrolo [1,2-a]indole.

15. 7 - Benzyloxy - 2,3-dihydro-9-formyl-1-oxo-1H-pyrrolo[1,2-a]indole.

16. 2,3 - Dihydro - 7 - methoxy - 6 - methyl - 1 - oxo - 1H - pyrrolo[1,2-a]indole-2-carbonitrile.

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